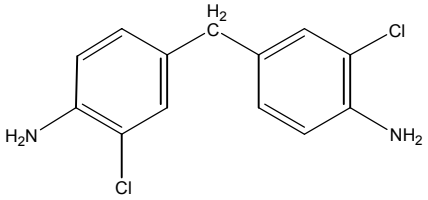
4,4′-METHYLENEBIS(2-CHLOROANILINE)
CAS No. 101-14-4
First Listed in the *Third Annual Report on Carcinogens*



CARCINOGENICITY

4,4′-Methylenebis(2-chloroaniline) (MBOCA) is *reasonably anticipated to be a human carcinogen* based on sufficient evidence of carcinogenicity of in experimental animals (IARC V.4, 1974; IARC S.7, 1987). When administered in the diet, 4,4′-methylenebis(2-chloroaniline) increased the incidences of hemangiosarcomas in mice of both sexes and hepatomas in female mice. When administered in the diet, MBOCA induced lung adenomas and adenocarcinomas and some mesotheliomas in rats of both sexes. In another study, when administered in the diet, MBOCA induced pulmonary adenomas, mammary adenocarcinomas, Zymbal gland carcinomas, and hepatocellular carcinomas in male rats. When administered by gavage, MBOCA induced transitional cell carcinomas of the urinary bladder in dogs. When administered by subcutaneous injection, MBOCA induced liver cell carcinomas and lung carcinomas in rats of both sexes.

There is inadequate evidence for the carcinogenicity of 4,4′-methylenebis(2-chloroaniline) in humans. In a review, a higher than expected incidence of urinary bladder cancer was reported among workers in a UK plant manufacturing MBOCA. An earlier study of workers manufacturing this compound in the United States, who were followed up for fewer than 16 years, failed to reveal any urinary bladder tumor (IARC S.7, 1987).

PROPERTIES

4,4′-Methylenebis(2-chloroaniline) is composed of colorless crystals. It is only slightly soluble in water but soluble in alcohol, ether, most organic solvents, and lipids. When heated to decomposition, it emits toxic fumes of hydrochloric acid and other chlorinated compounds as well as nitrogen oxides (NO_x). 4,4′-Methylenebis(2-chloroaniline) was commercially available in pellet, liquid, and granular form and as a premixed compound with polyhydric alcohols.

USE

4,4′-Methylenebis(2-chloroaniline) has been used as a curing agent in urethane and epoxy resin systems containing isocyanates, which are used to manufacture products such as integral-skin polyurethane semirigid foam for crash padding and solid urethane rubber moldings (e.g., gear blanks and industrial tires). Other uses for 4,4′-methylenebis(2-chloroaniline) include the manufacture of gun mounts, jet engine turbine blades, radar systems, and home appliances. In the laboratory, 4,4′-methylenebis(2-chloroaniline) is a model compound for studying carcinogens (IARC V.4, 1974).

PRODUCTION

There are no current production data available for 4,4′-methylenebis(2-chloroaniline). Chem Sources identified one bulk supplier among (Chem Sources, 1991). More than 1.9 million lb of 4,4′-methylenebis(2-chloroaniline) were imported into the United States in 1989 (USDOC Imports, 1990). Reports received by EPA in early 1983 indicated that U.S. manufacturers no longer produced 4,4′-methylenebis(2-chloroaniline) and that any 4,4′-methylenebis(2-chloroaniline) used is imported. The 1982 Directory of Chemical Producers indicated that one U.S. company produced 4,4′-methylenebis(2-chloroaniline) but no production data are available (SRI, 1982). CPSC also reported one manufacturer in 1981. 4,4′-Methylenebis(2-chloroaniline) was not reported to the USITC from 1980 to 1986 (USITC, 1987); in 1979, however, two producers reported 4,4′-methylenebis(2-chloroaniline) production, with an implied total production of more than 10,000 lb (USITC, 1980). The 1979 TSCA Inventory identified four companies producing 11 million lb of 4,4′-methylenebis(2-chloroaniline) and one company importing 55,000 lb in 1977. The CBI Aggregate was between 1 million and 100 million lb (TSCA, 1979). In 1977, the EPA identified five producers and importers of 4,4′-methylenebis(2-chloroaniline) in two regions, with a domestic production of 369,000 lb; no imports were reported. Production of 4,4′-methylenebis(2-chloroaniline) first was reported the United States in 1956 (IARC V.4, 1974).

EXPOSURE

The primary routes of potential human exposure to 4,4′-methylenebis(2-chloroaniline) are inhalation, dermal contact, and ingestion. Persons with the greatest possible risk of exposure to 4,4′-methylenebis(2-chloroaniline) were those persons involved in the manufacture of polyurethane and plastic products during the curing process. This accounted for 99% of all domestic uses (CHIP, 1981c). When used as a curing agent, 4,4′-methylenebis(2-chloroaniline) is melted before mixing into elastomer formulation and possibly could volatilize and be emitted into waste gases and wastewater from plants where it is being used. In 1971, investigators detected 4,4′-methylenebis(2-chloroaniline) in all samples of soil that were obtained within a three-quarter mile radius of a chemical plant in Adrian, Michigan. Some samples taken from soil on public roads in the area contained more than 500 ppm 4,4′-methylenebis(2-chloroaniline). Sludge from the Adrian wastewater treatment plant contained as much as 86 ppm 4,4′-methylenebis(2-chloroaniline), and samples of sludge obtained from the industrial lagoon contained 2,000 ppm. Urine from workers at the plant contained concentrations as high as 49 ppm of 4,4′-methylenebis(2-chloroaniline) per liter of urine (IARC V.4, 1974). The National Occupational Hazard Survey, conducted by NIOSH from 1972 to 1974, estimated that 33,000 workers were possibly exposed to 4,4′-methylenebis(2-chloroaniline) in the workplace (NIOSH, 1976). The recommended threshold limit value time-weighted average (TLV-TWA) for MBOCA is 0.02 ppm, and ACGIH considers it a suspected carcinogen and notes the potential for skin absorption (ACGIH, 1986). CPSC reported that residual levels of 4,4′-methylenebis(2-chloroaniline) may be present in final products, such as polyurethane foam and other plastic components. However, data describing actual levels of impurities and the potential for consumer exposure are lacking. The Toxic Chemical Release Inventory (EPA) listed seven industrial facilities that produced, processed, or otherwise used MBOCA in 1988 (TRI, 1990). In compliance with the Community Right-to-Know Program, the facilities reported releases of MBOCA to the environment which were estimated to total 750 lb. Additional exposure information may be found in the ATSDR Toxicological Profile for 4,4′-Methylenebis(2-chloroaniline) (ATSDR, 1994g).

REGULATIONS

EPA regulates 4,4′-methylenebis(2-chloroaniline) under the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA), Resource Conservation and Recovery Act (RCRA), and Toxic Substances Control Act (TSCA). Under CERCLA, EPA established a reportable quantity (RQ) of 10 lb and under RCRA designates 4,4′-methylenebis(2-chloroaniline) as a hazardous constituent of waste subject to report and recordkeeping requirements. Under TSCA, data are to be collected, and any new uses for 4,4′-methylenebis(2-chloroaniline) are to be reported. FDA prohibits the use of 4,4′-methylenebis(2-chloroaniline) in human food. NIOSH recommended an exposure limit of 0.003 mg/m^3 as a 10-hr time-weighted average (TWA) (skin). The OSHA standard for 4,4′-methylenebis(2-chloroaniline) was suspended by court action in 1974. The states of California, Michigan, and Kentucky have taken separate actions on 4,4′-methylenebis(2-chloroaniline) that were not affected by the court action. The OSHA permissible exposure limit (PEL) is 0.02 ppm as an 8-hr TWA. OSHA also regulates MBOCA under the Hazard Communication Standard and as a chemical hazard in laboratories. Regulations are summarized in Volume II, Table B-80.